

Medicare Coverage ~ Clinical Trials

Proposed National Coverage Decision

Clinical trials are research studies designed to evaluate the safety and effectiveness of medical care. They are key to understanding the appropriate use of medical interventions of all types and informing payers about what services to cover. All trials are based on a set of rules called a protocol. The protocol describes the characteristics of people who may be enrolled; the characteristics of people who may not participate; the length of the study; the schedule of tests, procedures, medications and dosages; and other study details.

Previously, Medicare has not paid for items and services related to clinical trials because of their experimental nature, i.e., their unknown benefits and potential risks to Medicare beneficiaries. One result of this policy has been a lack of information about the safety and effectiveness of medical interventions for the Medicare population. In fact, only a very small percentage of American seniors participate in clinical trials, although the elderly bear a disproportionate burden of disease in the United States. The absence of Medicare coverage has been a contributing factor to these low participation rates by the elderly.

On June 7, 2000, the President of the United States issued an executive memorandum directing the Secretary of Health and Human Services to "explicitly authorize [Medicare] payment for routine patient care costs...and costs due to medical complications associated with participation in clinical trials."

In keeping with the President's directive, this NCD serves to define the routine costs of clinical trials and identify the clinical trials for which payment for such routine costs should be made.

Definition of Routine Costs of Clinical Trials

For purposes of this national coverage decision, routine costs of a clinical trial include all items and services that are otherwise generally available to Medicare beneficiaries (e.g., hospital services, physician services, diagnostic tests) that are provided in a clinical trial except

- * the investigational item or service, itself,
- * items and services provided solely to satisfy data collection needs (protocol induced costs); and
- * items and services provided by the trial sponsor without charge.

For further clarification, routine costs that will be covered in clinical trials include:

- * Items or services that are typically provided absent a clinical trial (e.g., conventional care);
- * Items or services required solely for the provision of the investigational item or service (e.g., administration of a noncovered chemotherapeutic agent), the clinically appropriate monitoring of the effects of the item or service, or the prevention of complications; and
- * Items or services needed for reasonable and necessary care arising from the provision of an investigational item or service--in particular, for the diagnosis or treatment of complications.

In its recent report, *Extending Medicare Reimbursement in Clinical Trials*, the Institute of Medicine (IOM) defines routine costs of clinical trials as "care that would be received by a patient undergoing standard treatment. This would include such items as room and board for patients who are hospitalized, diagnostic and laboratory tests and monitoring appropriate to the patient's condition, post-surgical care when indicated, office visits, and so on." The IOM report specifically recommends excluding from Medicare coverage the investigational item or service, itself, and protocol-induced costs. The IOM defines protocol-induced costs as "patient care costs incurred in a clinical trial for services necessary solely to satisfy data collection needs of the clinical trial, such as monthly CT scans for a condition usually requiring only a single scan. Care that would be required under standard treatment--even if it also is required by the trial protocol--would not be considered protocol-induced." Thus, our proposed policy is consistent with the IOM's definition.

Definition of Clinical Trial for Purposes of Medicare Coverage

In order to implement this proposed coverage policy for routine costs in clinical trials, Medicare must define the clinical trials for which payment should be made. Therefore, we must develop a way to identify trials that meet an appropriate standard of quality and for which it is appropriate for Medicare to pay for associated routine costs.

We propose that all clinical trials must meet certain requirements in order for Medicare to pay for associated routine costs. As with Medicare coverage for any item or service, the subject of the trial must evaluate an item or service that falls within a Medicare benefit category (e.g., physicians' service, durable medical equipment, diagnostic test) and is not statutorily excluded from coverage (e.g., cosmetic surgery, hearing aids). Trials that are designed exclusively to test such things as toxicity levels or basic disease biology are excluded from coverage of routine costs. Trials of therapeutic interventions must enroll patients with diagnosed disease rather than healthy volunteers.

Trials funded by certain Federal agencies, as described below, will be automatically deemed to receive Medicare coverage of routine costs as soon as this NCD takes effect. Other types of trials will be included later as the principal investigators certify that the trials meet criteria developed by a Federal multi-agency group that are based on the

desirable characteristics that follow. The certification process will be simple and not pose a significant burden to the sponsors and investigators in the trials that are not deemed.

The proposed desirable characteristics of a trial are:

1. The principal purpose of the trial is to test whether the intervention potentially improves the participants' health outcomes;
2. The trial is well-supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use;
3. The trial does not unjustifiably duplicate existing studies;
4. The trial design is appropriate to answer the research question being asked in the trial;
5. The trial is sponsored by a credible organization or individual capable of executing the proposed trial successfully;
6. The trial is in compliance with Federal regulations relating to the protection of human subjects; and
7. The trial is conducted according to appropriate standards of scientific integrity.

For trials that do not have deemed approval status, we propose that a Federal multi-agency group, external to CMS, identify criteria that indicate that a trial is likely to have these desirable characteristics. We propose that the Agency for Healthcare Research and Quality (AHRQ) convene a multi-agency Federal group composed of representatives of the Department of Health and Human Services research agencies (National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), AHRQ, and the Office of Human Research Protection), and the research arms of the Department of Defense (DOD) and the Department of Veterans Affairs (VA). This multi-agency group would develop qualifying criteria that indicate a strong probability that a trial exhibits the desirable characteristics listed above. These criteria should be easily verifiable, and where possible, dichotomous. The multi-agency group will not approve trials. Trials that meet the qualifying criteria developed by the multi-agency group would receive Medicare coverage of their associated routine costs. The qualifying criteria would be developed under the authority found in §1142 of the Social Security Act (Act) (cross-referenced in §1862(a)(1)(E) of the Act).

A trial's principal investigator would submit a certification form indicating which of the qualifying criteria the trial meets and a copy of the trial protocol to a Medicare clinical trials registry. If the completed certification form demonstrates that the trial meets the criteria, the registry would assign a trial identifier to it. This identifier would allow the routine costs of the trial to be billed to Medicare. The Medicare clinical trials registry will be designed to protect patient confidentiality.

The multi-agency group would meet periodically to review and evaluate the program and recommend any necessary refinements to CMS. CMS would fund the administrative costs of this multi-agency group and the development and maintenance of the clinical trials registry through an interagency agreement with AHRQ.

As discussed above, certain trials are presumed to be of sound quality and would automatically be deemed to receive Medicare coverage of their associated routine costs. Trials funded by NIH, CDC, AHRQ, CMS, DOD, and VA, trials conducted at National Cancer Institute cancer centers, and all trials of patients that are either conducted under an investigational new drug application (IND) or are exempt from having an IND under 21 CFR 312.2(b)(1) would have deemed status. The trials' principal investigators would be required to enroll the trial in the Medicare clinical trials registry for tracking purposes. All other trials would be required to meet the qualifying criteria established by the multi-agency group.

This approach of automatically including certain trials and establishing a self-certification approval process for others will avoid the administrative burden that a trial-by-trial review would impose on the Federal government and trial investigators. A significant percentage of trials have already gone through an intensive peer-review process to obtain approval or funding by other entities.

CMS would accept all approvals arising from this self-certification process unless CMS's Chief Clinical Officer subsequently finds that a clinical trial does not meet the qualifying criteria or jeopardizes the safety or welfare of Medicare beneficiaries. We anticipate that such disapprovals would be rare.

Should CMS find that a trial's principal investigator misrepresented that the trial met the necessary qualifying criteria in order to gain approval for Medicare payment of its associated routine costs, Medicare coverage of the routine costs would be denied under §1862(a)(1)(E) of the Act. In the case of such a denial, the Medicare beneficiaries enrolled in the trial would not be held liable (i.e., would be held harmless from collection) for the costs consistent with the provisions of §1879, §1842(l), or §1834(j)(4) of the Act, as applicable. In such cases, the billing providers would be held liable for the costs. Trial sponsors and principal investigators may contractually handle liability issues. Where appropriate, fraud investigations of the billing providers and the trial's principal investigator may be pursued. Billing providers, of course, may avail themselves of existing procedures to appeal any adverse CMS action.

We are soliciting comments about what qualifying criteria might be appropriate and adequate to capture the desirable characteristics of a trial. The criteria should be easily verifiable and, where possible, dichotomous (that is, objective yes/no responses). Some examples might be:

- Is the trial approved by an investigational review board (IRB)?
- Does the trial have a written protocol?
- Has the trial been approved by a Federal agency?
- Has the trial received any external, non-Federal funding?
- Has the trial been reviewed by any external, non-Federal group?
- Does a data safety and monitoring board provide independent oversight of the trial?

The qualifying criteria suggested by commenters on this NCD will be forwarded to the multi-agency group once it is convened.

Details on coding and payment methodology where current claims processing systems are inadequate to support implementation of this NCD will accompany publication of the final NCD. Proper implementation of such payment methodologies may require rulemaking. Moreover, we intend to initiate a rulemaking to make the category A and B investigational device exemption (IDE) policy consistent with this NCD once it is finalized. Rulemaking will ensure that trials studying category A devices will be able to receive coverage of routine costs, as defined by this NCD.

Following final publication of this NCD, we will provide further clarification about how to identify properly which costs are routine patient care ones and which costs are protocol-induced ones. As part of that clarification, we may require that a trial's principal investigator and sponsors submit further material to the Medicare clinical trials registry. Examples of what we may request are a declaration of protocol-induced costs and a list of items and services being provided by the trial sponsor. For tracking purposes, we will probably also require a list of Medicare beneficiaries enrolled in the trial. Such information would be handled to ensure beneficiary confidentiality.

Impact on Medicare+Choice

Medicare regulations (42 C.F.R. §422.101(b)) require Medicare+Choice (M+C) organizations to follow CMS's national coverage decisions. This proposed NCD would establish Medicare coverage for certain items and services furnished as part of clinical trials that have the characteristics described above.

Except under certain specific circumstances (e.g., emergency care), M+C organizations furnish, or pay for, items and services covered under original Medicare only within the limits of a plan's rules governing the plan's network of providers and out-of-network referrals. For example, M+C organizations are not required to pay for services covered under original Medicare if a plan enrollee obtains covered services outside a plan's network without obtaining a pre-approval or referral required by the plan.

This NCD raises special issues that require some modification of the usual rules governing provision of items and services in and out of network in the M+C organization context. The items and services covered under this NCD are inextricably linked to the clinical trials with which they are associated and cannot be covered outside of the context of those clinical trials. However, an M+C organization typically will not have in its network all of the providers that participate in the clinical trials that are described in this NCD. To the extent that providers participating in clinical trials are within an M+C organization's network, the M+C organization can and should provide items and services within its network in accordance with this NCD. However, because an M+C organization is obligated to cover the items and services covered under this NCD, if a provider that participates in a clinical trial is not part of the M+C organization's network, the M+C

organization must provide items and services out-of-network in accordance with this NCD.

At the same time, we recognize the essential role of plans in the appropriate management and coordination of beneficiary health care. Thus, plans may have reporting requirements when enrollees participate in clinical trials that allow them to coordinate care appropriately. Plans are free to use their current tracking systems or develop new ones but they cannot require prior approval or prior authorization such services.

Medicare regulations (42 C.F.R. §422.109) also provide that, if CMS were to determine that an NCD meets the criteria for "significant cost," M+C organizations would not be required to bear the risk for the costs of the items and services covered under an NCD until the capitation rates are redetermined on a basis that incorporates those costs. Rather, the M+C organizations would be required to furnish, arrange, or pay for the items and services in the interim period, and obtain reimbursement from the Medicare fiscal intermediary and/or carrier in accordance with the original Medicare payment rules, methods, and requirements. CMS's Office of the Actuary is analyzing whether this NCD meets the criteria for "significant cost." In determining whether this NCD meets the criteria for "significant cost," CMS will take into account the additional costs to M+C organizations deriving from the requirement to pay for the items and services covered under this NCD outside of plan networks.

We welcome any public comments on the impact of this national coverage decision on Medicare+Choice plans.

Summary

A new section will be created in the Medicare Coverage Issues manual to implement this national coverage decision. Additional operating instructions will also be developed and published in the Medicare Carrier Manual and the Medicare Intermediary Manual. Other Medicare manuals will be modified, as appropriate. This national coverage policy is based upon the authority found in §1862(a)(1)(E) of the Social Security Act (Act). It is binding on all Medicare carriers, fiscal intermediaries, Peer Review Organizations, Health Maintenance Organizations, Competitive Medical Plans, Health Care Prepayment Plans, and Medicare+Choice organizations (§1852 (a)(1)(A) of the Act). In addition, an administrative law judge may not disregard, set aside, or otherwise review a national coverage decision issued under §1862(a)(1) of the Act. 42 C.F.R. § 405.860. We propose that the instruction read as follows:

Coverage of Items and Services Associated with Approved Clinical Trials

Medicare will pay for routine costs of approved clinical trials, as such costs are defined below, and will continue to pay for reasonable and necessary items and services to diagnose and treat complications arising from participation in all clinical trials.

Routine costs of a clinical trial include all items and services that are otherwise generally available to Medicare beneficiaries (e.g., hospital services, physician services, diagnostic tests) that are provided in a clinical trial except

- the investigational item or service, itself,
- items and services provided solely to satisfy data collection needs (protocol induced costs); and
- items and services provided by the trial sponsor without charge.

Routine costs in clinical trials include:

- Items or services that are typically provided absent a clinical trial (e.g., conventional care);
- Items or services required solely for the provision of the investigational item or service (e.g., administration of a noncovered chemotherapeutic agent), the clinically appropriate monitoring of the effects of the item or service, or the prevention of complications; and
- Items or services needed for reasonable and necessary care arising from the provision of an investigational item or service--in particular, for the diagnosis or treatment of complications.

For purposes of this policy, protocol-induced costs are patient care costs incurred in a clinical trial for items and services necessary solely to satisfy the data collection needs of the clinical trial, such as monthly CT scans for a condition usually requiring only a single scan. Care that would otherwise be required (i.e., conventional care)--even if it also were required by the trial protocol--is not considered protocol-induced.

For noncovered items and services, other than approved clinical trials, and including items and services for which Medicare payment is statutorily prohibited, Medicare only covers the treatment of complications arising from the delivery of the noncovered item or service and unrelated reasonable and necessary care. However, if the item or service is noncovered by virtue of a noncoverage policy in the Coverage Issues Manual and is the focus of an approved clinical trial, the routine costs of the clinical trial (as defined above) will be covered by Medicare but the noncovered service, itself, remains noncovered.

Requirements for Trial Approval for Medicare Coverage of Routine Costs

As with Medicare coverage for any item or service, the subject of the trial must evaluate an item or service that falls within a Medicare benefit category (e.g., physicians' service, durable medical equipment, diagnostic test) and is not statutorily excluded from coverage (e.g., cosmetic surgery, hearing aids). Trials that are designed exclusively to test such things as toxicity or basic disease biology are excluded from coverage. Additionally, trials of therapeutic interventions must enroll patients with diagnosed disease rather than healthy volunteers. All trials, including those with deemed approval status, must meet the above three requirements.

Trials should have the following desirable characteristics:

1. The principal purpose of the trial is to test whether the intervention potentially improves the participants' health outcomes;
2. The trial is well-supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use;
3. The trial does not unjustifiably duplicate existing studies;
4. The trial design is appropriate to answer the research question being asked in the trial;
5. The trial is sponsored by a credible organization or individual capable of executing the proposed trial successfully;
6. The trial is in compliance with Federal regulations relating to the protection of human subjects; and
7. All aspects of the trial are conducted according to the appropriate standards of scientific integrity.

Approval Process for Clinical Trials

Using the authority found in §1142 of the Act (cross-referenced in §1862(a)(1)(E) of the Act), the Agency for Healthcare Research and Quality (AHRQ) will convene a multi-agency Federal group composed of representatives of the Department of Health and Human Services research agencies (National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), AHRQ, and the Office of Human Research Protection), and the research arms of the Department of Defense (DOD) and the Department of Veterans Affairs (VA) to develop qualifying criteria that will indicate a strong probability that a trial exhibits the desirable characteristics listed above. These criteria should be easily verifiable, and where possible, dichotomous. Trials that meet these qualifying criteria will receive Medicare coverage of their associated routine costs. This multi-agency group is not approving trials. The trial's principal investigator will submit a certification form indicating which of the qualifying criteria the trial meets and a copy of the trial protocol to a Medicare clinical trials registry. If the completed certification form demonstrates that the trial should be approved, the registry will assign a unique identifier to it. This identifier will allow the routine costs of the trial to be billed to Medicare. The multi-agency group will meet periodically to review and evaluate the program and recommend any necessary refinements to CMS.

Some trials are automatically deemed to receive Medicare coverage of their associated routine costs. Trials funded by the National Institutes of Health, the Centers for Disease Control and Prevention, the Agency for Healthcare Research and Quality, the Centers for Medicare and Medicaid Services, the Department of Defense, and the Department of Veterans Affairs, trials conducted at National Cancer Institute cancer centers, and all trials of patients that are either conducted under an investigational new drug application (IND) or are exempt from having an IND under 21 CFR 312.2(b)(1) have deemed status. The trials' principal investigators do not need to self-certify but must enroll the trial in the Medicare clinical trials registry for tracking purposes.

CMS will accept all approvals arising from application of the self-certification process unless CMS's Chief Clinical Officer subsequently finds that a clinical trial does not meet the qualifying criteria or jeopardizes the safety or welfare of Medicare beneficiaries.

Should CMS find that a trial's principal investigator misrepresented that the trial met the necessary qualifying criteria in order to gain approval for Medicare payment of its associated routine costs, Medicare coverage of the routine costs would be denied under §1862(a)(1)(E) of the Act. In the case of such a denial, the Medicare beneficiaries enrolled in the trial would not be held liable (i.e., would be held harmless from collection) for the costs consistent with the provisions of §1879, §1842(l), or §1834(j)(4) of the Act, as applicable. In such cases, the billing providers would be held liable for the costs. Where appropriate, fraud investigations of the billing providers and the trial's principal investigator may be pursued.